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CARBON DIOXIDE RETENTION DURING PROLONGED EXPOSURE TO HIGH PRESSURE ENVIRONMENT

by

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and James H. Dougherty, M.S.

Bureau of Medicine and Surgery, Navy Department
Research Work Unit MF011.99-9003.02

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COMMANDING OFFICER
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SUBMARINE MEDICAL RESEARCH LABORATORY
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SUMMARY PAGE

THE PROBLEM

To complete a study of respiratory gas exchange during a 12-day exposure to seven atmospheres of pressure in an artificial atmosphere (Helium, Oxygen, and Nitrogen), which was undertaken in preparation for SEALAB II project.

FINDINGS

Evidence is presented for a CO_2 retention under resting conditions, as indicated by elevated alveolar CO_2 tensions and increased pulmonary and urinary CO_2 excretion. The observed CO_2 retention is interpreted as a summation of effects of accumulated CO_2 in the atmosphere, increased work of breathing, and respiratory pattern of trained diving personnel.

APPLICATIONS

Carbon dioxide retention is an ever-present problem to men engaged in underwater operations. The present report will contribute some information to a field (hyperbaric environment) where very few studies of gaseous exchange under these conditions have been carried out.

ADMINISTRATIVE INFORMATION

This investigation was conducted as a part of Bureau of Medicine and Surgery Research Work Unit MF011.99-9003—Physiological Effects of Long Duration Habitation in Hyperbaric Air and Artificial Environments. The present report is No. 2 on this Work Unit. It was approved for publication on 2 April 1968, and designated as Submarine Medical Research Laboratory Report No. 520.

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ABSTRACT

As part of the preparation for the SEALAB II project, three subjects were exposed for twelve days to seven atmospheres of pressure in an artificial environment composed of helium, oxygen and nitrogen. Average ambient CO_2 concentration was 1.17% surface equivalent. Resting respiratory minute volume was increased to twice normal and related to a proportional increase in tidal volume. Both oxygen consumption and CO_2 excretion were elevated, resulting in a respiratory exchange ratio of 1.02. Alveolar CO_2 and mixed expired CO_2 were significantly higher during the exposure period. Urine CO_2 excretion was markedly increased from the second day on throughout the exposure. Potassium, sodium and chloride excretion showed a transitory increase during the first four days. The pattern of urinary CO_2 and electrolyte excretion reflected a response to higher CO_2 load than that present in the atmosphere of the chamber during the test. All values returned to initial levels during the 27½ hour decompression period.

The observed CO_2 retention is explained as the summation of increased respiratory work indicated in the 38% reduction in maximum breathing capacity, accumulated CO_2 in the chamber atmosphere, and respiratory pattern of trained divers serving as subjects. A stress response was indicated in the increased blood corticosterone levels and elevated excretion of ketosteroids. The PO_2 level of 200 mm Hg did not produce any change in hemoglobin or hematocrit.

CARBON DIOXIDE RETENTION DURING PROLONGED EXPOSURE TO HIGH PRESSURE ENVIRONMENT

INTRODUCTION

Carbon dioxide (CO_2) retention seems to be the unwanted steady companion of underwater operations. Adaptation to breathhold diving was found to be associated with CO_2 retention and increased tolerance to CO_2.[31] Trained underwater swimmers and divers showed remarkable CO_2 retention and surprisingly high alveolar CO_2 values during moderate exercise.[13, 19] Interestingly, it is the training effect in underwater work and the resulting adaptation that predisposes the subjects to CO_2 retention.

Carbon dioxide intoxication has been implemented as the cause of "shallow water blackout" in men using closed circuit oxygen breathing apparatus.[2] Bennett[3] recently suggested hypercapnia as a possible cause of neuromuscular symptoms experienced by divers at 600 and 800 feet, breathing helium-oxygen mixtures. Because of its similarity with symptoms noted in "shallow water blackout," he coined the term "deep water blackout." Moreover, CO_2 retention is known to facilitate nitrogen narcosis and oxygen toxicity.

In spite of the obvious importance of CO_2 retention in the hyperbaric environment, very few studies have been carried out on gas exchange under these conditions. Because of their operational nature, most of the recent saturation-diving experiments did not include measurements of CO_2 excretion and O_2 consumption[1,4] with the exception of the two-day saturation at 650 feet, reported by Hamilton.[14] The present report deals with a study of respiratory gas exchange during a 12-day exposure to seven atmospheres $He\text{-}O_2\text{-}N_2$, which was undertaken in preparation for Sea Lab II. Although the scope of the investigation is limited, evidence is presented for a CO_2 retention under resting conditions which is explained as a summation of effects of accumulated CO_2 in the atmosphere, increased work of breathing, and respiratory pattern of trained diving personnel.

METHODS

Three subjects were confined in a chamber for 12 days under 7 atmospheres absolute pressure, breathing an atmosphere containing helium ($P_{I_{He}}$ 4680 mm Hg), oxygen ($P_{I_{02}}$ 205 mm Hg), nitrogen ($P_{I_{N2}}$ 302 mm Hg) and carbon dioxide ($P_{I_{C02}}$ 8.8 mm Hg). Two experienced U. S. Navy divers and one submarine medical officer served as subjects. All had considerable experience in diving techniques, and were fully acquainted with the hazardous nature of the experiment After the subjects entered the chamber (volume: 30 cubic meters), the door was closed and the room air present in the chamber was compressed with helium from high pressure cylinders to seven atmospheres within three hours. The concentration of helium, nitrogen, oxygen, and carbon dioxide in the chamber atmosphere were monitored with a Perkin-Elmer gas chromatograph, Beckman Model E paramegnetic oxygen analyzer and Beckman LBI infrared CO_2 analyzer. Frequent checks were made with the Scholander gas analysis apparatus. The partial pressures of the different ambient gases during the experiment are shown in Figure

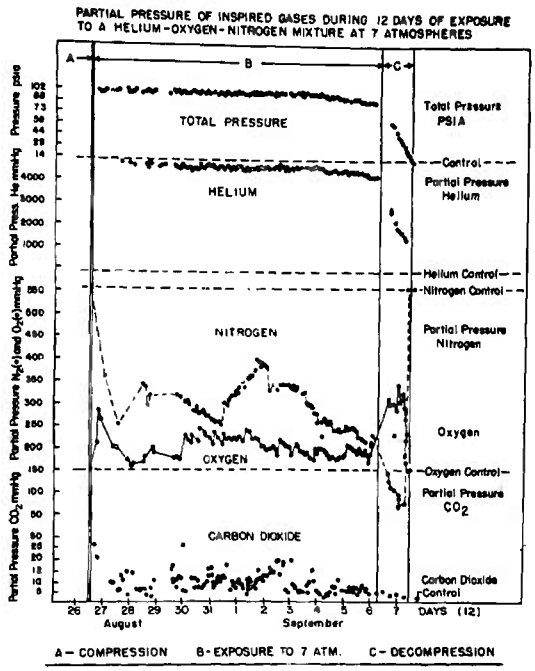

Figure 1. Partial pressures of ambient gases, helium, nitrogen, oxygen and carbon dioxide during 12-day exposure to 7 atmospheres absolute pressure.

1. The oxygen tension was kept at 200 mm Hg. The carbon dioxide tension was maintained at an average 8.8 mm Hg (1.17% sea level equivalent) by a lithium hydroxide absorption system. Respiratory minute volume was determined under resting condition by collecting exhaled air for a period of ten minutes in Douglas bags. The volume was measured with a dry gas meter inside the chamber. Mixed expired air from the Douglas bags was collected in evacuated steel cylinders. The latter filled under seven atmosphere pressures, contained enough gas for analysis with three instruments at normal atmospheric presure: Gas chromatograph, Scholander apparatus and Mass spectrometer (Naval Research Laboratory). Tidal volume was determined from tracings on the Collins respirometer.

Alveolar gas samples were obtained using a two-bag system previously employed in diving studies,[37] and also brought to the surface with evacuated steel cylinders. Venous blood samples (about 50 cc) were obtained by the physician inside the chamber, who had trained another member of the team to draw blood from him. The blood samples were decompressed in the medical lock, which frequently resulted in some hemolysis.

Measurements of blood pH and blood gases were not carried out due to difficulties in transfer of blood samples from seven atmospheres to one atmosphere. Hematocrit, hemoglobin, total number leucocytes and blood morphology were determined on an aliquot of each blood sample. Twenty-four hour urine specimens were collected in polyethylene bottles under oil, and aliquots of urine specimens in polyethylene bottles containing 5ml 6N HCl and were frozen until analyzed. Urine catecholamines, norepinephrine and epinephrine were isolated from the urines by adsorption on aluminum oxide at pH 7.4 and eluted with 0.2N acetic acid as described by Crout[12] with the following modification — acid elution of the catechol amines from the alumina was carried out in the suction funnel instead of using the column described. Fluorimetric estimation was by the trihydroxyindol method, using ferricyanide for oxidation as described by U. S. von Euler and I. Floding.[40] Fluorescence was measured on the Aminco-Kiers Phosphorimeter with the fluorescence attachment using blanks to which no $K3Fe(CN)_6$ was added. Seventeen-ketosteroids were determined by a modified Zimmerman procedure.[5] Urinary seventeen-hydroxysteroids were hydrolyzed from the conjugates with eight-glucuronidase (bacterial) at pH 6 and the cortisteroids extracted with chloroform. The chromogens were developed by a modified Porter-Silber procedure and a control was run to compensate for non-steroid chromogenic substances present in the urine.[6] Blood corticosteroids were measured by the Silber-Busch-Oslapas fluorimetric method.[39] Hydrocortisone was determined by the method described by Peterson[27] and based on the method of Peterson, Karrer and Guerra.[28] Spectrophotometric measurements were made on the Beckman Spinco 151 Spectrocolorimeter at 410 Mu.

In the afternoon of the 2nd, 4th, 6th and 9th day of exposure to high pressure the subjects performed standard step-up tests

(20 times in 30 seconds) and 20 standard push-ups.

During the entire experimental period the subjects kept a watch schedule, one man always remained awake and on duty. Outside the chamber, a medical officer and two chamber operators were in constant attendance. A standby pressure system was available in the event of accidental, explosive decompression.

The decompression was carried out on a continuous schedule, rather than a stage decompression, lasting twenty-seven and one-half hours.

RESULTS

Subjective experiences

The subjects tolerated the exposure to this hyperbaric environment well. The atmosphere felt cool and damp and the temperature inside the chamber had to be raised to 30° C to provide more comfort. The relative humidity was kept at around 75%. During the first few days there was marked emotional tension which was reflected in the metabolic stress response. The weight of all subjects did not change significantly.

Pulmonary gas exchange

Data on respiratory minute volume, tidal volume and maximum breathing capacity are shown in Figure 2. Maximum breathing capacity decreased 38% on exposure to seven atmospheres, which gives an indication of the increased breathing resistance. Respiratory minute volume and tidal volume increased, both approximately twofold, during exposure to high pressure. However, the increased ventilation was not apparently sufficient to prevent carbon dioxide retention, which is expressed in the rise of alveolar CO_2 tension, and the increase in pulmonary as well as urinary CO_2 excretion (Figure 3, Table I).

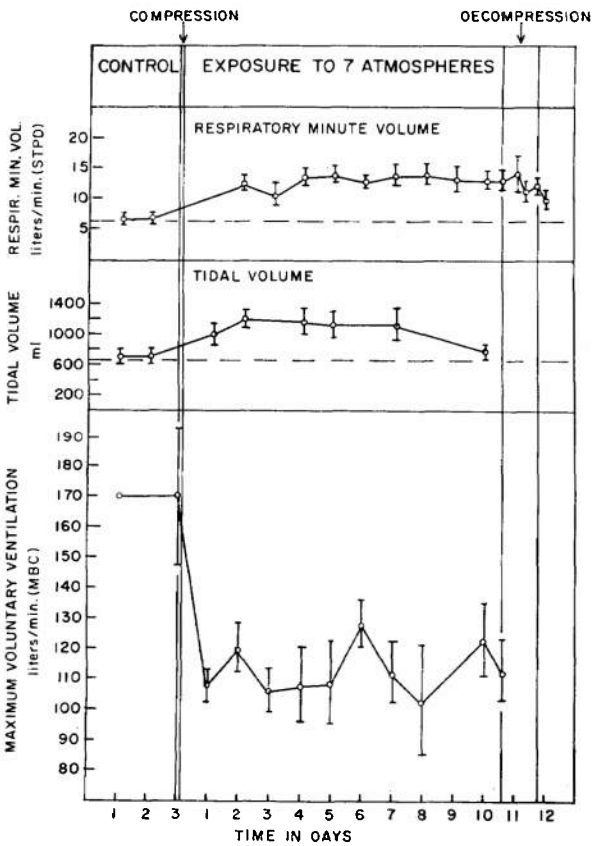

Figure 2. Effect of prolonged exposure to helium-oxygen-nitrogen mixture at 7 atmospheres on respiratory minute volume, tidal volume and maximum breathing capacity.

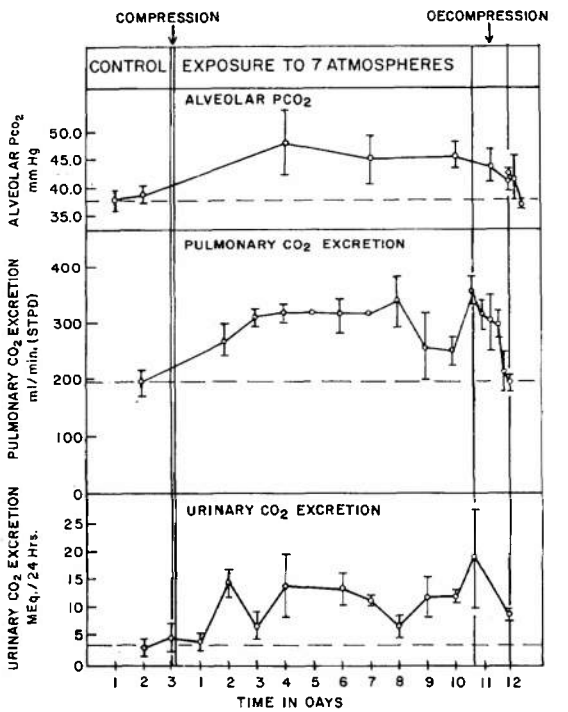

Figure 3. Alveolar CO_2 tension, pulmonary CO_2 excretion and urinary CO_2 excretion during prolonged exposure to 7 atmospheres of He-0_2-N_2.

TABLE I.

EFFECT OF PROLONGED EXPOSURE TO 7 ATMOSPHERES ($He-O_2-N_2$) ON RESPIRATORY MINUTE VOLUME, TIDAL VOLUME, ALVEOLAR P_{CO_2}, MIXED EXPIRED P_{CO_2}, CO_2 DEAD SPACE, V_{CO_2}, V_{O_2} AND RQ IN MEN

		Control	Exposure to 7 atm. ($He-O_2N_2$)	Decompression 27.5 hours
Respiratory Minute Volume BTPS Liter/min	Mean	6.65 (6)	13.62* (22)	11.86* (13)
	S.D.	.82	2.57	2.9
Tidal Volume Liter	Mean	.70 (3)	1.11* (19)	—
	S.D.	.14	.24	—
Alveolar P_{CO_2} mm Hg	Mean	38.3 (6)	45.1* (9)	40.8 (8)
	S.D.	2.3	5.0	3.34
Mixed Expired CO_2 mm Hg	Mean	26.5 (3)	29.8* (39)	26.4 (14)
	S.D.	1.3	5.0	3.4
CO_2 Dead Space Liter	Mean	.19 (3)	.37* (9)	—
	S.D.	.03	.08	—
V_{CO_2} STPD ℓ/min	Mean	.20 (3)	.31* (22)	.29 (11)
	S.D.	.02	.05	.05
V_{O_2} STPD ℓ/min	Mean	.23 (3)	.30* (22)	.31 (8)
	S.D.	.01	.05	.07
RQ	Mean	.85 (3)	1.02* (22)	.91 (8)
	S.D.	.06	.11	.12

* Differences from controls statistically significant at the 5% level and better

( ) Represents number of determinations

Mixed expiration CO_2 was also markedly elevated during the exposure period but not during the decompression time. The calculated CO_2 dead space (using alveolar and mixed expired CO_2 values with the Bohr equation) was found greatly increased, Table I.

The increase in carbon dioxide excretion (54%) was higher than the corresponding rise in oxygen consumption (30%) resulting in a respiratory exchange ratio greater than one.

Urinary excretion

Urine volume, urine pH, as well as urinary excretion of sodium, potassium, chloride, and phosphorus tended to increase during exposure to high pressure and during the decompression period without reaching statistically significant values. However, carbon dioxide, nitrogen, ammonia, and calcium excretion were found to be significantly elevated, Table II.

TABLE II.
EFFECT OF PROLONGED EXPOSURE TO 7 ATMOSPHERES ($He-O_2-N_2$) ON URINARY EXCRETION OF CO_2, ELECTROLYTES, TOTAL NITROGEN, AMMONIA, AND TITRATABLE ACIDITY

		Control		Exposure		Decompression	
Urine Volume ml/24 hours	Mean	1652.5	(8)	2108.4	(31)	2705.	(3)
	S.D.	696.7		1142.2		1530.	
Specific Gravity	Mean	1.02	(8)	1.02	(31)	1.01	(3)
	S.D.	.01		.01		.01	
pH	Mean	5.87	(8)	5.98	(31)	5.73	(3)
	S.D.	.34		.43		.18	
CO_2 mEq/24 hours	Mean	3.47	(6)	11.06*	(31)	8.26	(3)
	S.D.	2.81		19.2		1.04	
Na mEq/24 hours	Mean	141.67	(8)	185.08	(31)	216.8	(3)
	S.D	56.8		106.7		65.	
K mEq/24 hours	Mean	55.6	(8)	65.7	(31)	81.5	(3)
	S.D.	16.7		27.8		18.9	
Cl mEq/24 hours	Mean	160.9	(8)	182.4	(31)	195.6	(3)
	S.D.	65.9		69.7		51.9	
Ca mEq/24 hours	Mean	.08	(8)	.14*	(31)	.16	(3)
	S.D.	.05		.07		.84	
P mEq/24 hours	Mean	.98	(8)	1.18	(31)	1.54	(3)
	S.D	.27		.55		.39	
Urine nitrogen g/24 hours	Mean	10.89	(8)	15.24*	(31)	17.56*	(3)
	S.D.	4.02		6.03		2.2	(3)
Ammonia mg/24 hours	Mean	297.2	(8)	465.5*	(31)	507.6	(3)
	S.D	116.4		207.8		161.7	
Titratable Acidity ml 0.1 N NaOH/ 24 hours	Mean	395.8	(8)	503.8*	(31)	418.5	(3)
	S.D.	106.1		112.9		118.7	

* Differences from controls statistically significant at the 5% level and better

( ) Represents number of determinations

Daily changes in urinary excretion, displayed in Figures 4 and 5, exhibit a transitory increase in potassium sodium and chloride excretion during the first four days while carbon dioxide excretion remains elevated throughout the exposure period, Figure 4. Total nitrogen and ammonia excretion showed the same pattern as carbon dioxide excretion. Figure 5.

Urinary catechol amines (epinephrine and norepinephrine), as well as 17-hydroxysteroids, were not affected by exposure to seven atmospheres, Table III. However, 17-ketosteroid excretion showed a significant rise which started somewhat belatedly on the third day and lasted throughout the rest of the exposure to high pressure and the decompression period, Figure 6.

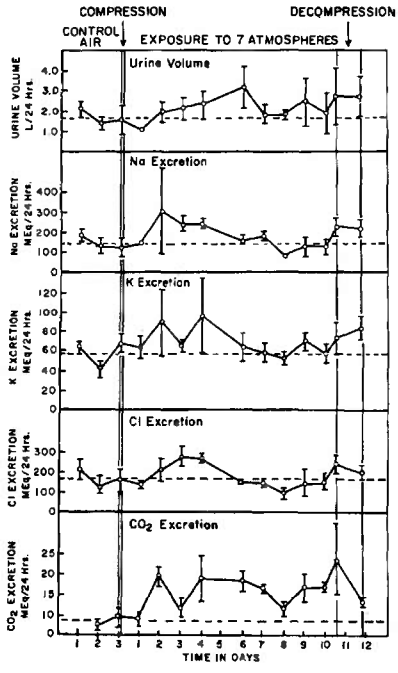

Figure 4. Urine volume and electrolyte excretion (Na, K, Cl, CO_2) during prolonged exposure to 7 atmospheres of He-O_2-N_2.

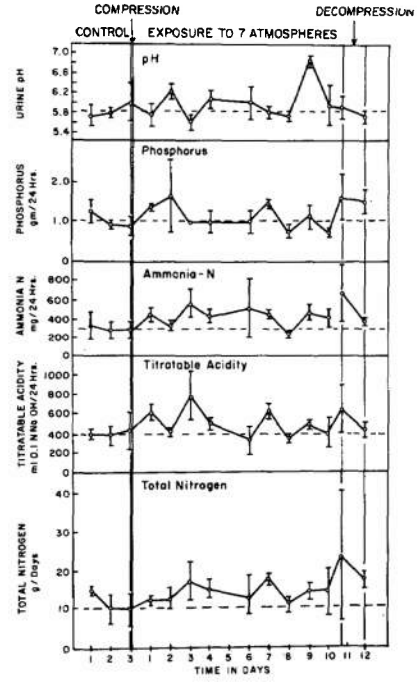

Figure 5. Effect of prolonged exposure to 7 atmospheres (He-O_2-N_2) on urinary pH and urinary phosphorus, ammonia, titratable acidity and total nitrogen.

TABLE III.
EFFECT OF PROLONGED EXPOSURE TO SEVEN ATMOSPHERES PRESSURE ON EXCRETION OF CATECHOLAMINES AND STEROIDS

		Control		Exposure		Decompression	
Epinephrine	Mean	6.2	(8)	7.1	(28)	10.7	(3)
μg/24 hours	S.D.	1.5		2.1		6.4	
Norepinephrine	Mean	13.5	(8)	17.2	(28)	16.1	(3)
μg/24 hours	S.D.	5.8		6.1		2.2	
17-Ketosteroids	Mean	16.7	(8)	25.9*	(31)	29.8	(3)
mg/24 hours	S.D.	7.8		12.8		14.6	
17-OH Ketosteroids	Mean	3.48	(8)	3.19	(31)	2.67	(3)
mg/24 hours	S.D	1.62		1.26		1.25	

* Differences from controls statistically significant at the 5% level and better

( ) Represents number of determinations

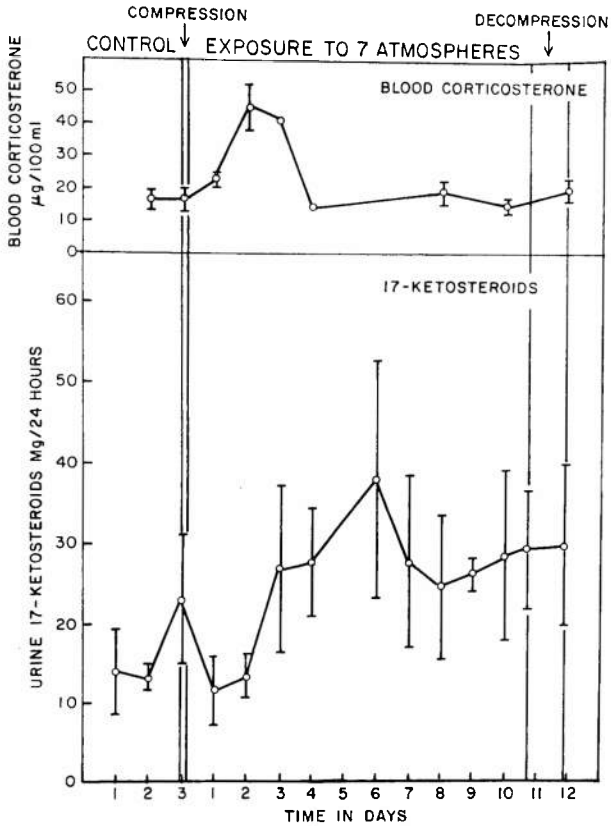

Figure 6. Effect of prolonged exposure to 7 atmospheres ($He\text{-}0_2\text{-}N_2$) on blood corticosterone levels and 17-ketosteroid excretion.

Blood chemistry and haemetological values

There were no changes in plasma electrolytes during exposure to high pressure with the exception of small but significant decrease in plasma potassium. Glucose and BUN did not change but blood corticosterone increased significantly. This increase was limited to the first four days, Figure 6.

Hemoglobin and hematocrit did not change while the total number of leucocytes increased during exposure to high pressure, Table V.

The subjects remained, during the whole period, in good physical condition, which is expressed in that fact that the cardiovascular scores following standard step-up tests did not change during exposure to high pressure. (Control at one atmosphere 209.3 ± 28.4 (n = 3) ; Experimental under high pressure 215.8 ± 13.4 (n = 12).*

Electrocardiogram

During the first three days under pressure, two subjects showed an elevation of the S-T segment in leads I, II, V_5 and V_6 of the standard 12 lead electrocardiogram. These changes disappeared after three days.

* The reported mean values of cardiovascular scores following standard step-up tests were calculated from data obtained by Lynch, J. I.: Exercise Tolerance Studies in an Artificial Atmosphere under Increased Barometric Pressure. MRL Rept. No. 419, January, 1964

TABLE IV.

EFFECT OF PROLONGED EXPOSURE TO SEVEN ATMOSPHERES ($He-O_2-N_2$) ON PLASMA ELECTROLYTES, BUN, GLUCOSE AND CORTICOSTERONE

		Control		Exposure		Decompression	
Na mEq/L Plasma	Mean	138.4	(3)	137.1	(18)	144.5	(3)
	S.D.	2.9		8.6		6.2	
K mEq/L Plasma	Mean	4.9	(3)	4.5*	(17)	4.4	(3)
	S.D	.2		.44		.26	
Cl mEq/L Plasma	Mean	106	(3)	104.8	(17)	104.5	(3)
	S.D.	2		2.2		0	
Ca Mg/100 ml	Mean	—		10	(17)	8.9	(3)
	S.D.	—		.9		.8	
Inorganic Phosphorus Mg/100 ml	Mean	3.4	(3)	3.4	(17)	3.8	(3)
	S.D.	.6		.5		.2	
BUN Mg/100 ml	Mean	15.3	(3)	13.5	(20)	—	
	S.D.	2.8		3		—	
Glucose Mg/100 ml	Mean	69	(3)	76.6	(20)	—	
	S.D	5.7		11.6		—	
Corticosterone Mg/100 ml	Mean	16.7	(3)	26.9*	(17)	20	(3)
	S.D	4.5		13.6		4.4	

* Differences from controls statistically significant at the 5% level and better

( ) Represents number of determinations

TABLE V.

EFFECT OF PROLONGED EXPOSURE TO 7 ATMOSPHERES ($He-O_2-N_2$) ON TOTAL NUMBER OF WBC, NEUTROPHILS, LYMPHOCYTES, HEMATOCRIT AND HEMOGLOBIN

		Control		Exposure		Decompression
Total WBC	Mean	5267	(3)	6230*	(20)	—
	S.D	2.08.2		331.9		
Total Neutrophils	Mean	3171	(3)	3760	(20)	—
	S.D.	433		890		
Total Lymphocytes	Mean	2007	(3)	2334	(20)	—
	S.D.	510		643		
Hematocrit	Mean	44	(3)	41.7	(20)	—
	S.D	2.8		1.6		
Hemoglobin g/100 ml	Mean	14.4	(3)	13.9	(20)	—
	S.D.	.6		.5		

* Differences from controls statistically significant at the 5% level and better

( ) Represents number of determinations

DISCUSSION

In view of the well known difficulties in obtaining reliable and repeatable measurements of ventilation and respiratory gases under increased pressures, it appears necessary to evaluate the validity of the methods used in this experiment.

The Collins respirometer, which was used for measurements of maximum breathing capacity and tidal volume reported in this paper, has also been employed by Wood[42] in high pressure studies and was found to give results which were in good agreement with those obtained with the Wedge spirometer under the same conditions.[20] Lanphier[21] reported a value of 105 liters for maximum breathing capacity determined by Maio and Farhi[24] at 7.5 atmospheres while breathing an 80% helium-20% oxygen mixture, which is in line with our results of 107 liters at seven atmospheres in 89.6% helium, 3.6% oxygen and 5% nitrogen. The system employed for the measurement of resting respiratory minute volume, consisting of low resistance Hans-Rudolph valve and a Douglas bag and dry gas meter in the chamber, did not offer any significant resistance to influence the results. The main difficulties, connected with the transfer and decompression of respiratory gas samples from high pressure to normal atmospheric pressure, were avoided by collection of mixed expired samples from the Douglas bag and alveolar gas samples from anesthesia bags into evacuated steel cylinders. Any method of collecting alveolar gas samples under high pressure using a respiratory valve is subject to criticism because the breathing resistance, already increased by the high gas density, will be further elevated and might result in too high CO_2 values. Influence of this kind cannot be excluded with the two-bag, small dead space system used. But further considerations, given below, indicate that the alveolar CO_2 values are approximately in the right order.

In most high pressure experiments and diving operations there is an interaction of a number of factors, such as increased gas density resulting in restriction of ventilation, narcotic effects of nitrogen, depressing effects of increased oxygen tensions on ventilation, effects of accumulated CO_2 in the atmosphere. It is, therefore, quite difficult to clarify the role of the individual factors. We are fortunate to have two complicating factors eliminated in this experiment, namely, nitrogen narcosis and oxygen effects. Nitrogen tension is reduced to half normal and oxygen tension at 200 mm Hg is only slightly elevated above normal.

Respiratory Work

Under our experimental conditions, the calculated gas density was 1.5 times that of air while the viscosity of the gas mixture was only slightly increased to 1.13 times that of air. It has been amply demonstrated that increased gas density increases the air way resistance.[7, 25, 26] This increase in airway resistance is thought to be caused by an increase in turbulent flow which rises with increased gas density according to Reynold's number.[7] A proportional increase in alveolar pressure is required to move the gas under increased pressure[24] resulting in more respiratory work.

Results of measurements of flow rates and lung functions obtained in this experiment have been reported in a previous communication.[23] Data on maximum breathing capacity have been included in Figure 2 to demonstrate relations to other respiratory functions. The 38% reduction in maximum breathing capacity is a measure of the increased respiratory work. Resting ventilation was found elevated (100%), which must have been accomplished by an increase in tidal volume since the latter increased proportionally to ventilation.

High alveolar CO_2 values under high pressure have been found by a number of investigators[17, 19] but they were only observed during exertion and not under resting conditions. Additional factors must therefore be considered which would cause the elevation of resting alveolar CO_2 tension.

The increase in tidal volume under high pressure is in line with respiratory changes reported by Hesser.[17] The oxygen cost of breathing a twice normal volume is increased, as indicated in the 30% rise in oxygen consumption. Wood[42] has suggested that the

efficiency of respiratory muscles in hyperbaric states might be comparable to that of the emphysematous patient, who also has a similar alteration in respiratory pattern consisting of an increase in tidal volume and decrease in respiratory rate. If this is true, the oxygen cost of moving the same volume of air would be markedly increased, as has been shown for the emphysematous patient.[10] Unfortunately, there are no data in the literature, to our knowledge, which compare the oxygen cost of breathing at normal and increased pressure.

Another similarity with the emphysematous patient consists in the elevated alveolar CO_2 tension based on an increased dead space. Here the analogy ends because the second factor contributing to rise in alveolar CO_2 tension, the increased CO_2 production, is not present in emphysema patients.

The increase in breathing resistance, resulting in a 38% reduction in maximum voluntary ventilation, could explain an increase in alveolar P_{CO_2} during exertion. However there is sufficient ventilatory capacity left to provide for an adequate alveolar ventilation under resting conditions.

Effect of accumulated CO_2 in the High Pressure He-O_2 Atmosphere

The subjects were exposed for 12 days to an average CO_2 concentration of 1.17%. If we use, for a comparison, data obtained during prolonged exposure to 1.5% CO_2,[35] increases in both alveolar CO_2 and ventilation would be much less amounting to 40 mm Hg P_{CO_2} and a 38% increase in respiratory minute volume (9.23 ℓ/min compared with 13.6 ℓ/min). There is a much smaller increase in tidal volume (16%) and dead space (36%) during exposure to 1.5% CO_2 than under the conditions of this experiment. Nevertheless, the changes in ventilation and respiratory mechanics all go in the same direction. Obviously, the effect of exposure to 1.17% CO_2 is not sufficient to explain the extent of the observed changes in respiration.

Starting at the other end, we can ask what ventilatory response would correspond to the measured alveolar P_{CO_2} of 45.1 ± 5.0 mm Hg. Based on a large number of measurements on healthy subjects, we have previously established that at a P_{CO_2} of 46.4 ± 1.9 mm Hg, produced by inhalation of 5.5% CO_2, corresponded with a minute ventilation of 22.1 ± 6.4 liters/minute.[31] The alveolar P_{CO_2} data, obtained under normal atmospheric pressure, are in the range of those observed in this experiment and if used for a comparison we have to conclude that the ventilatory response to alveolar P_{CO_2} measured under seven atmospheres is significantly depressed. In other words, we deal with a CO_2 retention resulting in an alveolar P_{CO_2} which corresponds with an exposure to 5.5% CO_2. If this is true, one should find corresponding changes in the acid-base balance. Unfortunately, we could not carry out measurements of blood pH and blood gases due to difficulties in transfer of blood samples from seven atmospheres to one atmosphere. However, the urinary excretion data, shown in Figures 4, 5, and Table II, exhibit a response characteristic for a hypercapnia induced by higher CO_2 concentrations.

Potassium, sodium and chloride excretion were elevated during the first four days. This transitory increase in cation excretion and chloride excretion in the first phase of hypercapnia is in line with observations made in chronic hypercapnia induced by CO_2 concentrations ranging from 8-10% in dogs[29] and in rats.[8] It corresponds with the initial steep rise in plasma bicarbonate. As shown in Figure 5, urine pH was slightly elevated. Phosphate excretion showed an initial transitory rise, while ammonia and titratable acidity excretion was elevated throughout the exposure. Although the changes of NH_4 and titratable acidity are small, they are statistically significant (Table II) and are in accordance with a typical pattern observed in hypercapnia in dogs[29] and man[30] exposed to 3% CO_2.

The urine electrolyte excretion during prolonged exposure to 1.5% CO_2 showed a markedly different pattern than that observed in this experiment. During the first 24 days of uncompensated respiratory acidosis there was no elevation in potassium, sodium or chloride excretion nor an increase in carbon

dioxide excretion.[36] As a matter of fact, one of the most important findings of the 1.5% study was that the renal regulation was so different from that observed during exposure to higher CO_2 concentrations and that extra renal regulation, tissue CO_2 stores (bones with very long time constant) played a predominant role in the attainment of an equilibrium.

Although phosphate excretion was elevated during the first phase of uncompensated respiratory acidosis induced by exposure to 1.5% CO_2, calcium excretion remained unchanged and urinary nitrogen elimination declined. Under high pressure, both calcium and nitrogen excretion were found increased. Such changes are not observed in high or low CO_2. They could be related to reduction in physical activity, for which they are characteristic.[41]

The blood calcium remained at a normal level (Table IV which is in line with Hamilton's observation during exposure to 20 atmospheres He-0_2.[14]). However, Hartmann[16] reported a fall in blood calcium under 23 atmospheric He-0_2. In these two studies, urinary calcium excretion was not measured.

Respiratory pattern and CO_2 retention

Lanphier[19] found in his trained divers a group of "high CO_2 divers," who responded to moderate work under pressure with subnormal alveolar ventilation and surprisingly high alveolar CO_2 values. He further observed that external breathing resistance had little influence on the response. They also showed a reduced respiratory response to inhaled carbon dioxide, similar to the condition we reported in adaptation to diving in Submarine Escape Instructors.[33] In comparing trained and untrained underwater swimmers, Goff and Bartlett[13] noted a CO_2 build up exclusively in trained underwater swimmers and suggesting that their peculiar breathing pattern leads to a CO_2 retention. This is in line with our previous studies[34] demonstrating that the respiratory pattern determines the ventilatory response to CO_2. Subjects with a large tidal volume and small respiratory rate exhibit a higher alveolar CO_2 tension even under resting conditions and show a decrease in slope and shift to the right in the CO_2 response curve. Such a respiratory pattern and response curve to CO_2 are typical for trained divers[32] and were found to develop during adaptation to CO_2.[34] Since two of our subjects were trained divers and the third subject, a medical officer, had just finished a tour of duty which involved frequent breathhold diving at the Escape Training Tank, it is most likely that all the subjects belonged to the group of "CO_2 retainers," which is supported by the rather high control values of 0.7 liter tidal volume.

Since all three factors, accumulated CO_2 in the atmosphere, increased breathing resistance and respiratory pattern of trained divers, produce effects in the same direction resulting in a decreased alveolar ventilation and increased alveolar CO_2, it is reasonable to assume that the decreased alveolar ventilation and increased alveolar CO_2, found in this experiment under resting conditions, can be explained by the summation of effects of accumulated CO_2 in the atmosphere, increased breathing resistance and respiratory pattern of trained divers.

Additional findings

A stress response was observed but found to be limited to the adrenal cortex. A marked increase in blood corticosterones occurred during the first four days, and an elevation of 17-ketosteroids excretion which started later on the third day and lasted through the last day of the exposure period. However, epinephrine and norepinephrine did not change significantly.

The observed electrocardiographic changes occurred during the stress period of the first three days, which is marked by an increase in blood corticosterones. The alterations in the electrocardiogram have been interpreted as those occurring under stress[9] which is in agreement with similar findings of Hamilton[14] under pressure.

Hemoglobin and hematocrit did not change under these conditions, indicating that a 50 mm Hg increase in P_{O_2} to 200 mm Hg is tolerated without apparent changes in hematopoiesis. However, a seven-day exposure of two subjects to a twice normal pressure of

O_2 (300 mm Hg) in compressed air at 10.5 meters, studied by Cousteau and Alinat,[11] resulted in a significant decrease in total number of red cells associated with a fall in hematocrit in both subjects. It appears, therefore, that a P_{O_2} of 300 mm Hg is a threshold value concerning effects on hematopoieses. These findings have a bearing on the use of higher concentrations of oxygen under high pressure. In recent saturation-excursion dives, oxygen concentrations were frequently raised to 0.6 atmospheres, corresponding to 456 mm Hg. If the time periods of saturation-excursion dives are extended, effects on hematopoiesis may become pronounced.

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13. ABSTRACT

In preparation for the SEALAB II project, three subjects were exposed for twelve days to seven atmosphere of pressure in an artificial environment composed of helium, oxygen and nitrogen. Average ambient CO_2 concentration was 17% surface equivalent. Resting respiratory minute volume was increased to twice normal and related to a proportional increase in tidal volume. Both oxygen consumption and CO_2 excretion were elevated, resulting in a respiratory exchange ratio of 1.02. Alveolar CO_2 adn mixed expired CO_2 were significantly higher during the exposure period. Urine CO_2 excretion was markedly increased from the second day on throughout the exposure. Potassium, sodium and chloride excretion showed a transitory increase during the first four days. The pattern of urinary CO_2 and electrolyte excretion reflected a response to higher CO_2 load than that present in the atmosphere of the chamber during the test. All values returned to initial levels during the 27 1/2 hour decompression period.

The observed CO_2 retention is explained as the summation of increased respiratory work indicated in the 38% reduction in maximum creathing capacity, accumulated CO_2 in the chamber atmosphere, and respiratory pattern of trained divers serving as subjects. In regard to the increased CO_2 production, an additional factor of possible metabolic alterations is suggested. A stress response was indicated in the increased blood corticosterone levels and elevated excretion of ketosteroids. The PO_2 level of 200 mm Hg did not produce any change in hemoglobin or hematocrit.

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